

Ischemic skin lesions in ulcerative colitis

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Among the skin complications of idiopathic ulcerative colitis, pyoderma gangrenosum is probably the most severe but rarely results in cutaneous gangrene.¹ Superficial ischemia and gangrene of the skin not evidently associated with pyoderma gangrenosum is also a rare complication of ulcerative colitis²⁻⁵ and tends not to be recognized; we present two cases in which the digits were affected.

Case reports

Case 1

A 24-year-old woman was transferred to our hospital because of persistent diarrhea and rectal bleeding despite 2 weeks of treatment at another hospital with intravenously administered adrenocorticotropin (ACTH), as well as sulfasalazine, blood transfusions and total parenteral nutrition.

Crohn's disease had been diagnosed 4 years earlier on the basis of intermittent pain in the right lower quadrant of the abdomen, and she had since been treated with prednisone and sulfasalazine except during her two pregnancies. Recently her symptoms had become severe and intractable; barium enema roentgenography had shown mucosal irregularity in the rectosigmoid region, as well as mucosal edema, cobblestone formation and ulceration in the descending colon.

The patient now appeared wasted. Both lower quadrants of the abdomen were tender. Sigmoidoscopy

demonstrated diffusely edematous and friable mucosa, minor internal hemorrhoids and a posterior anal fissure.

In the patient's peripheral blood the hemoglobin level was 119 g/L and the leukocyte count $21.4 \times 10^9/L$ (50% of the cells were neutrophils and 36% band forms, and toxic granules were present). Although the platelet count ($377 \times 10^9/L$) and the prothrombin time (11.4 seconds) were normal, the partial thromboplastin time was slightly low, at 23 (in our laboratory normally 25 to 39) seconds. The blood glucose level was high, at 128 mg/dL (7.1 mmol/L). Serum protein electrophoresis revealed low levels of albumin (29.5 [normally 35 to 50] g/L) and β -globulin (2.8 [normally 6 to 13] g/L). All other biochemical tests of the blood gave results within normal limits. Stool cultures yielded normal flora, and blood cultures showed no growth. Abdominal and pelvic ultrasonography did not reveal an abscess.

The ACTH was replaced with hydrocortisone sodium succinate, also given intravenously; later oral prednisone therapy was used. The patient was not given sulfasalazine in our hospital. Further blood transfusions were required when acute lower intestinal bleeding recurred.

On the patient's 19th day in our hospital, pain, sensory deficit and ischemic changes (dark discoloration of the skin) developed in the toes of the left foot (Fig. 1). The skin of the right great toe also showed some mottled discoloration. The femoral, popliteal and posterior tibial pulses were all strong and equal, but the dorsalis pedis pulses were impalpable.

By this time the platelet count had risen to $578 \times 10^9/L$, and it later rose to $882 \times 10^9/L$. The plasma fibrinogen level was high, at 5.4 (normally 1.5 to 3.0) g/L. In the serum no cryoglobulins were detected, the IgG, IgA and IgM values were normal, and the levels of the third and fourth components of complement (C3 and C4) were low, at 0.35 and 0.10 g/L (normally 0.70 to 1.86 and 0.16 to 0.45 g/L respec-

tively), although the C4 level was normal (0.25 g/L) on one occasion. The arterial blood gas values were normal.

Barium meal roentgenography showed nondistensibility of the terminal ileum, thumb-printing and islands of filling defects in the cecum and throughout the colon, and a granular appearance of the rectal mucosa.

Repeated administration of 0.25% bupivacaine hydrochloride through an epidural catheter inserted between the third and fourth lumbar vertebrae provided partial relief of the pain in the patient's left toes, but there was no change in the skin's colour.

Because of the intractable severe bowel disease and its apparent relation to the ischemic changes in the toes, total proctocolectomy and ileostomy was performed 4 days after the changes appeared. The small bowel, including the terminal ileum, appeared normal, but the entire colonic mucosa was thickened and hyperemic. Pathological examination of the resected tissue showed that the entire serosal surface, the anal canal and perianal skin, and the mucosa of the terminal ileum were grossly normal. The mucosa of the cecum and the rectum was beefy red, with shallow ulcers. The mucosa of the colon was studded with polypoid structures ranging in diameter from 0.5 to 1.0 cm; sections revealed the typical histologic fea-

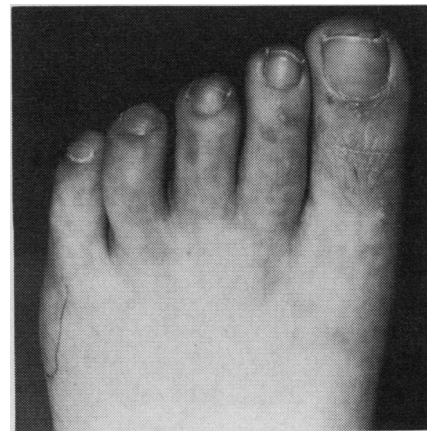


Fig. 1—Case 1: Dark discoloration of skin of left toes; skin of right great toe also showed some mottled discoloration.

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tures of ulcerative colitis and no granulomatous lesions (Fig. 2). Sections of the distal ileum showed mild, nonspecific inflammation, and sections of the anus showed thrombosed hemorrhoids.

Postoperatively a clear demarcation persisted between the dusky distal skin and the proximal normal skin of the left toes; the skin of the right great toe appeared normal. Epidural administration of bupivacaine was continued for several days. The patient was discharged on the 19th postoperative day.

Four months later the terminal phalanx of the second toe of the left foot had to be amputated because of necrotic changes. However, the patient was able to resume all of her usual activities within a month. Although the skin over the left toes had a normal colour when warm, it became purple when exposed to the cold; this feature was still present several months later, at the time of the last contact with the patient. The skin of the right foot was normal.

Case 2

A 43-year-old East Indian man who had come to Canada 10 years previously was seen because of a 3-month history of moderate bloody diarrhea and a 3-week history of progressive pain in the tips of all the fingers.

The patient appeared well nourished. His fingertips were cool and showed dusky mottled erythema extending from the anterior periungual area to the distal interphalangeal joint, as well as dusky discoloration of the nail bed (Fig. 3). The nails failed to blanch with pressure. The finger joints were normal.

The abdomen yielded no abnormal findings, but sigmoidoscopy showed marked diffuse edema, areas of intense hyperemia, and generalized fine granularity of the mucosa of the distal sigmoid colon and the rectum. A rectal biopsy revealed a marked increase in the numbers of chronic inflammatory cells in the lamina propria and distortion of the crypt architecture, with a few neutrophils in the crypt epithelium; early crypt abscesses were present.

In the peripheral blood the hemoglobin level, leukocyte count and platelet count were normal, but the erythrocyte sedimentation rate was high, at 67 mm/h. The prothrombin time (11.6 seconds) and the partial thromboplastin time (28.9 seconds) were normal, as was the blood glucose level (119 mg/dL [6.6 mmol/L]). Serum protein electrophoresis revealed a high level of γ -globulin (17.9 [normally 7 to 16] g/L); the serum level of IgG was also high (20.13 [normally 8 to 18] g/L). The serum C3 level was low, at 0.35 (normally 0.50 to 1.20) g/L,

and the C4 level high, at 0.74 (normally 0.16 to 0.45) g/L. A slide test for antinuclear antibody in the serum gave positive results at a titre of 1:40, but a latex fixation test for rheumatoid factor had negative results. Tests for parasites in the stools gave negative results, and stool cultures yielded only normal flora.

Treatment with sulfasalazine was followed by rapid resolution of the bloody diarrhea and gradual resolution of the pain and ischemic changes in the fingertips over about 4 weeks.

Discussion

Ulcerative colitis is associated with a hypercoagulable state, the features of which may include thrombocytosis, increased levels of fibrinogen and factors V and VII, and decreased levels of antithrombin III.⁶⁻⁷ Although thrombocytosis has been observed in acute inflammatory bowel disease,⁸ platelet counts of less than $1000 \times 10^9/L$ are rarely associated with thrombotic complications.⁹ Venous thrombosis is a recognized complication¹⁰ and arterial thrombosis an occasional complication^{11,12} of ulcerative colitis.

Occlusion of small blood vessels, causing localized ischemic and gangrenous changes in the skin, is a rare complication of ulcerative colitis.²⁻⁴ The suggested mechanisms in-

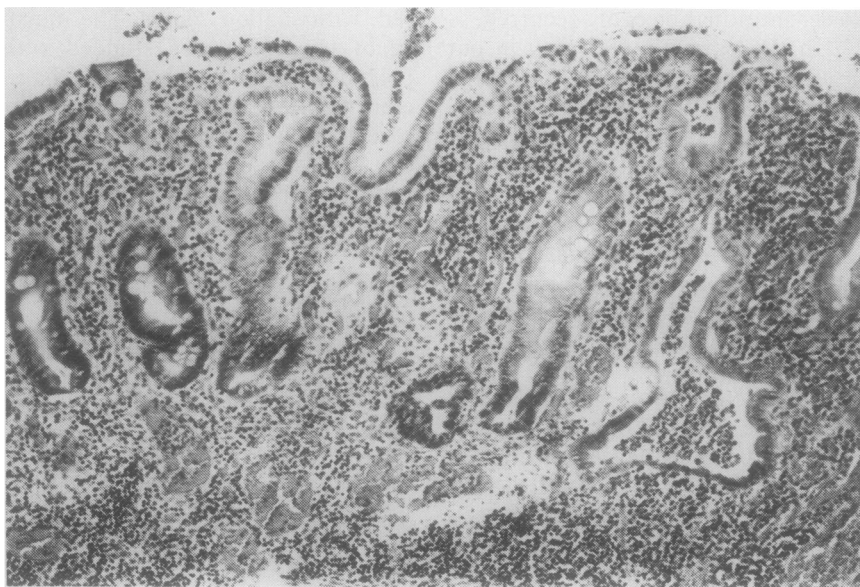


Fig. 2—Case 1: Typical features of chronic active ulcerative colitis: focal loss of surface epithelium, with exudate, collections of neutrophils in crypts, almost total loss of goblet cells, and dense infiltrate of lymphocytes and plasma cells in lamina propria (hematoxylin-eosin; $\times 60$, reduced one third).

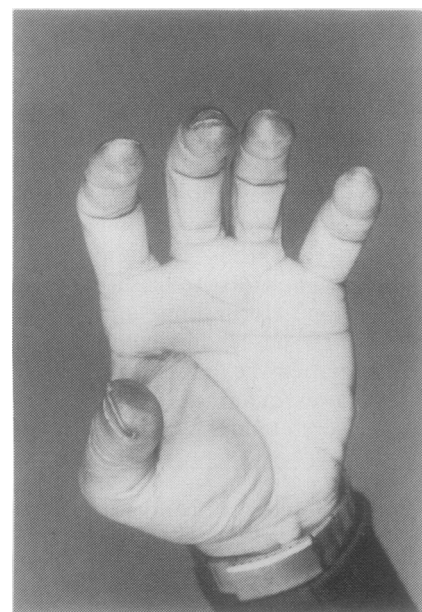


Fig. 3—Case 2: Dusky mottled discoloration of skin of all fingertips (seen also on left hand).

clude necrotizing cutaneous vasculitis induced by circulating antigen-antibody complexes,⁵ arterial and venous occlusions in the absence of necrotizing vasculitis,⁴ capillary and venous thrombosis,¹³ and cryofibrinogenemia accompanied by evidence of thrombosis of blood vessels.² Antigen-antibody complexes may be present in the serum of patients with ulcerative colitis.^{14,15} Cryofibrinogenemia is occasionally found in inflammatory states,² and the clinical manifestations of essential cryofibrinogenemia have included extensive gangrene of the extremities and buttocks.¹⁶ A role for corticosteroids in the thrombotic complications of ulcerative colitis has been rejected.¹⁷

In our first patient the ischemic skin changes began to resolve only after proctocolectomy, and then did so slowly; vasospasm in response to cold was evident a year after the operation. In the second patient the skin changes appeared to resolve in response to treatment with sulfasalazine, which quickly eradicated his bloody diarrhea.

The reason for the predilection for involvement of the digits in our two patients is unclear. Local vascular factors may influence the site of occurrence of the skin lesions in ulcerative colitis.

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PRECAUTIONS: As with other sulfonamide preparations, critical appraisal of benefit versus risk should be made in patients with liver damage, renal damage, urinary obstruction, blood dyscrasias, allergies or bronchial asthma. The possibility of a superinfection with a non-sensitive organism should be borne in mind.

DOSAGE AND ADMINISTRATION: Adults and children over 12 years. Standard dosage: 2 SEPTRA tablets or 1 SEPTRA DS tablet twice daily. Minimum dosage and dosage for long-term treatment: 1 SEPTRA tablet or 1/2 SEPTRA DS tablet twice daily. Maximum dosage. Overwhelming infections: 3 SEPTRA tablets or 1 1/2 SEPTRA DS tablets twice daily. Uncomplicated gonorrhea: 2 SEPTRA tablets or 1 SEPTRA DS tablet four times daily for 2 days.

Pneumocystis carinii pneumonia: 20 mg/kg/day trimethoprim and 100 mg/kg/day sulfamethoxazole in four divided doses for 14 days.

Children 12 years and under:†
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Children 2 to 5 years: 2.5-5 mL of suspension twice daily.

Children 6 to 12 years: 5-10 mL of suspension twice daily.

†In children this corresponds to an approximate dose of 6 mg trimethoprim/kg body weight/day, plus 30 mg sulfamethoxazole/kg body weight/day, divided into two equal doses.

DOSAGE FORMS:

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SEPTRA TABLETS, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole, and coded SEPTRA Y2B. Bottles of 100 and 500.

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SEPTRA FOR INFUSION, each ampoule (5 mL) containing 80 mg trimethoprim and 400 mg sulfamethoxazole.

Product Monograph available on request.

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